Applied Nursing Research 28 (2015) e1–e6

Contents lists available at ScienceDirect

Applied Nursing Research

journal homepage: www.elsevier.com/locate/apnr

Original Article

Relationships among psychosocial factors, biomarkers, preeclampsia, and preterm birth in African American women: A pilot

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ARTICLE INFO

Article history:
Received 17 February 2014
Revised 24 August 2014
Accepted 3 September 2014

Keywords:
Stress
Cytokines
Preeclampsia
Preterm birth

ABSTRACT

Aim: To explore the relationships among psychosocial factors (optimism, uncertainty, social support, coping, psychological distress), biomarkers (cortisol, cytokines), preeclampsia, and preterm birth in African American women.
Methods: Forty-nine pregnant African American women completed psychosocial questionnaires and had blood collected for biomarkers between 26 and 36 weeks of gestation. Birth outcomes were obtained from birth records.
Results: Women reporting higher levels of social support had lower levels of pro-inflammatory cytokines (IL-2, IL-5, and IL-6). Surprisingly, compared with low-risk pregnant women, women diagnosed with preeclampsia reported more optimism and less avoidance, and had lower levels of cortisol and IFN-γ. Similarly, compared to women with full-term birth, women with preterm birth reported higher levels of optimism and lower levels of avoidance, and had lower levels of IL-10.
Conclusion: Psychosocial factors influence inflammation and pregnancy outcomes. Close assessment and monitoring of psychosocial factors may contribute to improved pregnancy outcomes.

1. Introduction

In 2012, 11.54% of infants were born prematurely (<37 weeks of gestation) in the United States (Hamilton, Martin, & Ventura, 2013). Preterm birth is a major factor associated with neonatal mortality, developmental delays, school failure, and chronic illness (McCormick, Litt, Smith, & Zupancic, 2011). Moreover, preterm birth results in medical costs of over $26 billion per year in the United States (Institute of Medicine, 2006). Compared with non-Hispanic white women, African American women are 1.6 times more likely to have preterm birth (Hamilton et al., 2013).

Preeclampsia, one of the factors leading to preterm birth, is characterized by hypertension and proteinuria after 20 weeks of gestation (Mutter & Karumanchi, 2008). The incidence of preeclampsia in the general population in the United States is approximately 2%–5% of all pregnancies (Alfonso, 2009; Osterman, Martin, & Menacker, 2009; Redman, 2011). African American women tend to have higher rates of preeclampsia compared with non-Hispanic white women (e.g., 49.2 versus 44.0 cases per 1000 live births in 2008) (Osterman, Martin, Mathews, & Hamilton, 2011). However, racial differences in the incidence and severity of preeclampsia have been difficult to assess due to confounders of socioeconomic and cultural factors (Task force of hypertension in pregnancy, 2013).

Women with preeclampsia have higher levels of psychological stress compared with low-risk pregnant women (Black, 2007). Furthermore, women with higher levels of distress in early pregnancy are more likely to develop preeclampsia later in pregnancy (Kurki, Hiilesmaa, Raitasalo, Mattila, & Ylikorkala, 2000). Psychological stress is a known risk factor for preterm birth (Beydoun & Saftlas, 2008; Hobel, Goldstein, & Barrett, 2008). However, such risk may be attenuated by protective psychosocial factors, like optimism, coping, and social support, which are known to reduce psychological distress. For instance, in pregnant women high levels of optimism and social support, and low levels of uncertainty and avoidance, have been related to lower levels of psychological distress (Giurgescu, Penckofer, Maurer, & Bryant, 2006; Lobel, Yali, Zhu, DeVinvent, & Meyer, 2002; Yali & Lobel, 2002). These protective factors appear to buffer the negative effects of psychological distress on preeclampsia and preterm birth, possibly through modulatory effects on inflammation.

Psychological stress activates the hypothalamic–pituitary–adrenal axis (HPA) resulting in the sequential secretion of corticotrophin

There is no conflict of interest.

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http://dx.doi.org/10.1016/j.apnr.2014.09.002
0897-1897/

releasing hormone (CRH) from the hypothalamus, adrenocorticotropic hormone (ACTH) from the anterior pituitary and cortisol from the adrenal cortex (Hobel, 2004). Bi-directional signaling occurs between the HPA axis and the immune system. For example, pro-inflammatory cytokines such as interleukin-1 beta (IL-1β), IL-6, and tumor necrosis factor-alpha (TNF-α) stimulate the HPA axis and increase the output of cortisol (Kunz-Ebrecht, Mohamed-Ali, Fledman, Kirschbaum, & Steptoe, 2003; Witek-Janusek & Mathews, 2000). Cortisol down-regulates these same pro-inflammatory cytokines (Geiss, Varadi, Steinback, Bauer, & Anton, 1997) and stimulates the production of anti-inflammatory cytokines such as IL-1 receptor antagonist (IL-1ra) and soluble TNF-receptor 2 (sTNF-RII) (Barber et al., 1995; Elenkov & Chrousos, 2002), thereby limiting inflammatory responses. During chronic stress, however, cortisol is less effective at suppressing the immune system and inflammation (Elenkov & Chrousos, 2002; Gennaro & Hennessy, 2003; Ruiz, Fullerton, & Dudley, 2003), in part due to a reduced responsiveness of glucocorticoid receptors on immune cells. Hence, higher continuous levels of stress have been related to higher levels of pro-inflammatory cytokines, and lower levels of anti-inflammatory cytokines (Coussons-Read, Okun, & Nettles, 2007; Coussons-Read, Okun, Schmitt, & Giese, 2005).

Preeclampsia could develop when the systemic inflammatory process causes the maternal system to decompensate (Redman, 2011). Women with preeclampsia may have greater alterations in cortisol and cytokine secretions than low-risk pregnant women. Notably, women diagnosed with preeclampsia have higher basal levels of cortisol (Heilmann, Buchheim, Wacker, & Ziegler, 2001) and serum pro-inflammatory cytokines (e.g., IL-1β, IL-6, IL-8, TNF-α) (Casart, Tarrazzi, & Camejo, 2007; Jonsson et al., 2006; Kalinderis et al., 2011; Tosun et al., 2010) compared with low-risk pregnant women. High cortisol levels (Erickson et al., 2001; Field et al., 2004; Hobel, Dunkel-Schetter, Roesch, Castro, & Arora, 1999; Kramer et al., 2010; Sandman et al., 2006) and a state of low grade inflammation characterized by higher serum levels of IL-1β, IL-6, IL-8 and TNF-α (Hasegawa et al., 2003; Vogel et al., 2007) have been associated with increased risk for preterm birth. Indeed, a recent systematic review found that women with preterm birth have increased levels of pro-inflammatory cytokines during pregnancy, particularly IL-6, IL-1β and TNF- α compared with women with full term birth (Lyon et al., 2010). Such a pro-inflammatory environment, due to either increased production of pro-inflammatory cytokines or decreased production of anti-inflammatory cytokines, may be instrumental in the etiology of preterm birth (Mulherin Engel, Erichsen et al., 2005; Mulherin Engel, Olshan, et al., 2005).

Numerous researchers have examined the potential individual relationships among psychosocial factors (optimism, uncertainty, social support, coping strategies, psychological distress), biological markers (cortisol, cytokines), and pregnancy outcomes (preeclampsia, preterm birth). These findings have demonstrated that women with preeclampsia and preterm birth have higher average levels of psychological distress, cortisol and inflammation, which are accompanied by lower levels of protective factors, such as personal resources. However, there are no reports in the literature which have examined the relationships among all of these factors within a single investigation. Guided by the Stress and Coping Transactional Model (Lazarus & Folkman, 1984) and the framework of Psychoneuroimmunology (PNI) (Ader & Kelley, 2007) the purpose of this pilot study was to explore the relationships among psychosocial factors, biomarkers, preeclampsia, and preterm birth in a sample of pregnant African American women.

2. Methods

2.1. Design and sample

A cross-sectional comparative correlational design was conducted to (1) examine the relationships among psychosocial factors and biomarkers; (2) explore differences in these variables between (a) low-risk pregnant women versus women diagnosed with preeclampsia, and (b) women with full term birth versus preterm birth; and (3) estimate the probability of preterm birth and preeclampsia. This pilot study was conducted at the outpatient clinics of two medical centers in Chicago that provide level III obstetrical care and are comparable in the population they serve. The sample was recruited from the midwifery and residency practices which serve mostly women from low socioeconomic status. The study was approved by Institutional Review Boards of the medical centers. We recruited two groups of pregnant women: 1) diagnosed with preeclampsia, and 2) medically low-risk. The inclusion criteria for both groups consisted of African American women 18 to 39 years of age, singleton pregnancy, and who were able to read English. We enrolled women between 24 and 37 weeks of gestation since infants born prior to 24 weeks are not viable and infants at 37 weeks or later are term. These inclusion criteria were selected because teen pregnant women, women with multiple pregnancies and those with non-viable fetuses may have higher psychological stress related to their situation. Exclusion criteria were diagnosis of HIV, autoimmune disorders, cancer, major depression, chronic hypertension, pregestational diabetes, or administration of steroids within the two weeks prior to data collection. These exclusion criteria were selected because these diagnoses and medications may influence the levels of cytokines. In this pilot we enrolled 12 women who were diagnosed with preeclampsia and 37 low risk pregnant women. The diagnosis of preeclampsia was made by the health care provider based on (1) elevated blood pressure (greater or equal to 140 mmHg systolic or greater or equal to 90 mmHg diastolic) after 20 weeks of gestation for women with prior normal blood pressure; and (2) proteinuria (greater than or equal to 300 mg of protein in 24 h urine collection) (Task force of hypertension in pregnancy, 2013). Women diagnosed with preeclampsia received antepartum testing once or twice weekly in addition to their routine prenatal visits.

2.2. Measures

The variables and instruments are presented in Table 1.

2.3. Research procedures

Pregnant African American women between 24 and 37 weeks of gestation were invited to participate by the health care providers at the participating sites. After giving informed consent, participants received and completed the packet of questionnaires in a private room after their prenatal visit. The participant's venous blood was drawn into an ethylenediaminetetraacetic acid (EDTA) coated sterile tube (10 ml) and placed on ice. This was done in the afternoon (1:00 p.m.–5:00 p.m.) to better control for circadian rhythm. Serum cortisol is increased in pregnant women, but the typical diurnal rhythm persists with higher values in the morning and more stable values in the afternoon. Many serum cytokines (e.g., pro-inflammatory) show a circadian rhythm opposite to that of cortisol, with highest values during sleep periods and lower values during wakefulness (Vgontzas & Chrousos, 2002; Vgontzas et al., 2005). After collection, samples were immediately transported on ice to a laboratory where they were centrifuged (1500 $g \times 15$ min at 4 °C), aliquoted (400 μl per tube), and stored at −80 °C. All assays were run in duplicate according to manufacturer specifications. The assays were conducted by the laboratory technician under the supervision of one of the co-authors of the study.

2.4. Data analysis

Analysis of biomarkers (IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IFN-γ, TNF-α, cortisol) was conducted for 46 of the participants. Two low-risk pregnant women and one woman with preeclampsia did not have blood drawn. Ten samples for IL-1β, six samples for IL-2, five samples for IL-4, one sample for IL-8, six samples for IFN-γ, and ten samples for TNF-α were below the limits of detection in duplicate wells. This